DNA ADDUCTS INDUCED BY ENVIRONMENTAL CHEMICALS

Bernadette Schoket

Department of Biochemistry, Johan Béla National Institute of Public Health, Budapest, H-1097 Hungary

Molecular events in chemical carcinogenesis involve the formation of DNA adducts of carcinogen metabolites but the relationship between this early event and later disease has not been fully elucidated. DNA adducts can be considered as molecular dosimeters for the assessment of the biologically effective dose resulting from genotoxic exposures.

Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous environmental pollutants and many of them are known carcinogens. Therefore, several studies have been carried out in occupational settings in which populations are exposed to complex mixtures of PAHs. Aromatic DNA adducts or PAH-DNA adducts have been investigated in white blood cells from coke-oven and iron foundry workers, roofers, firefighters, surface coating and aluminium plant workers. Adduct levels have been determined by ^{32}P-postlabelling, enzyme-linked immunosorbent assay, ultrasensitive radioimmunoassay and synchronous fluorescence spectrophotometry. Most of the studies have been cross-sectional and designed to investigate the relationship between exposure and DNA adduct levels. There have been large interindividual variations and in most cases enhanced levels of DNA adducts have been detected in exposed populations in comparison to controls. Dose-related adduct formation has been found in iron-foundry and coke-oven workers and roofers. A longitudinal study has been performed in two aluminium plants in Hungary on two occasions one year apart, in order to obtain information on temporal variability of exposure and its relationship to DNA adduct levels. A significant increase of adduct levels occurred in one of the plants from one year to the next which may have originated from a change of the workplace atmosphere at the period of the second sample collection.

More than 500 oil wells were set on fire in Kuwait in early 1991 which has produced a massive and unprecedented air pollution in the environment of the Persian Gulf region. Genotoxic effect of the chemically complex combustion material has been studied in white blood cell DNA of US personnel served in the region. Levels of aromatic DNA adducts determined by ^{32}P-postlabelling have not shown difference in a small group of individuals before and after the period of exposure. In a different investigation PAH-DNA adducts have been determined by dissociation-enhanced lanthanide fluoroimmunoassay before, during and after the period of exposure. Results have indicated elevated DNA adduct levels after the period of exposure in comparison to the previous two monitoring times.

DNA adducts are useful markers of genotoxic exposure on group basis. Recognition and quantitation of multiple adducts may vary with the methods applied. Therefore, adduct levels have to be considered relative between individuals and exposure groups. Investigation of DNA adducts may lead to a better understanding of mechanisms of chemical carcinogenesis and contribute to improved carcinogenic risk assessment.

R. f uttachel